

REMARKS

Claims 1 to 60 and 71 are all the claims pending in the application.

Claims 1-21 and 71 have been rejected under 35 U.S.C. § 103(a) as obvious over the Muller et al article in view of U.S. Patent 6,255,522 to Matsuo et al.

Applicants submit that Muller et al and Matsuo et al do not disclose or render obvious the subject matter of the above claims and, accordingly, request withdrawal of this rejection.

The present invention as set forth in claim 1 is directed to a process for producing an optically active  $\alpha$ -substituted aminoketone represented by formula (4) or an optically active  $\alpha$ -substituted aminoketone salt represented by formula (5), the process comprising the steps of reacting an  $\alpha$ -substituted ketone represented by formula (1) with an optically active amine represented by formula (2) to yield a mixture of diastereomers of an optically active  $\alpha$ -substituted aminoketone represented by formula (3) and isolating one diastereomer from the mixture after optionally yielding salts of the diastereomers with an acid.

By employing an optically active amine as set forth in claim 1, since the obtained aminoketone forms diastereomers, one diastereomer can be easily separated from the other. Therefore, an optically pure compound can be obtained.

As set forth in dependent claim 9, the acid can be methanesulfonic acid.

The present invention as set forth in independent claim 71 is directed to a process for producing an optically active  $\alpha$ -substituted aminoketone represented by formula (4) or an optically active  $\alpha$ -substituted aminoketone of formula (5) by isolating one diastereomer from the

mixture of diastereomers of an optically active  $\alpha$ -substituted aminoketone represented by formula (3) after optionally yielding salts of the diastereomers with an acid.

The Examiner particularly relies on the disclosure at page 451, lines 11-21 of Muller et al. The Examiner states that Muller et al teach a process for preparing stereoisomers of the aminoketone compound. The Examiner states the difference between Muller et al and the presently claimed invention is that Muller et al do not mention methanesulfonic acid for the preparation of stereoisomers.

The Examiner relies on Matsuo et al for a teaching of a process for preparing optically active aminoketones in which methanesulfonic acid is used in the preparation of the optically active aminoketone. The Examiner particularly refers to column 8 and the various Examples in Matsuo et al.

The Examiner argues that it would have been obvious to modify the Muller et al process by using the methanesulfonic acid disclosed in Matsuo et al because Matsuo et al expressly teach that the use of methanesulfonic acid is old in the art of making stereoisomers of aminoketones.

In response, applicants submit that Muller et al do not disclose a process for producing an optically active  $\alpha$ -substituted aminoketone of formula (4) or an optically active  $\alpha$ -substituted aminoketone salt of formula (5), and do not disclose or suggest the use of an optically active amine represented by formula (2) of the present claims.

To the extent that Muller et al disclose the use of an amine, Muller et al would be disclosing the use of a racemic amine, and not an optically active amine. Accordingly, the compounds disclosed in Muller et al would not be optically active.

In general, Muller et al do not disclose a process for producing a mixture of diastereomers of an optically active  $\alpha$ -substituted aminoketone of formula (3), and do not disclose the step of isolating an optically active compound from a mixture of diastereomers.

The compound 1b at pages 450 and 452 of Muller et al satisfies the structure of formula (3) of the present claims, but the compound 1b of Muller et al is not optically active.

Thus, Muller et al differ from the present invention as set forth in claim 1 because Muller et al do not disclose a process for producing an optically active  $\alpha$ -substituted aminoketone represented by formula (4) or the optically active  $\alpha$ -substituted aminoketone salt of formula (5), do not disclose or suggest employing an optically active amine represented by formula (2) to produce a mixture of diastereomers of an optically active  $\alpha$ -substituted aminoketone of formula (3), and do not disclose or suggest isolating one diastereomer from a mixture of diastereomers of an optically active  $\alpha$ -substituted aminoketone represented by formula (3) after optionally yielding salts of the diastereomers with an acid.

Further, with respect to claim 9, Muller et al do not disclose or suggest the use of methanesulfonic acid.

Similarly, with respect to claim 71, Muller et al do not disclose or suggest a process for producing an optically active  $\alpha$ -substituted aminoketone represented by formula (4) or an optically active  $\alpha$ -substituted aminoketone salt of formula (5), and do not disclose or suggest isolating one diastereomer from a mixture of diastereomers of an optically active  $\alpha$ -substituted aminoketone represented by formula (3) after optionally yielding salts of the diastereomers with an acid.

With respect to Matsuo et al, this patent discloses the use of methanesulfonic acid as a reactive ingredient which reacts with an organoaluminum compound of general formula (4) of Matsuo et al and an alcohol compound of general formula (6) of Matsuo et al to form a reducing agent. This reducing agent is then reacted with an aminoketone compound of general formula (1) of Matsuo et al to form an aminoalcohol of general formula (7) of Matsuo et al.

In the present invention, the acid is optionally employed to isolate one diastereomer from a mixture of diastereomers of an optically active aminoketone by preparing a salt of the compound of formula (3) with an acid. Matsuo et al do not disclose the use of an acid to prepare a salt of a compound of formula (3) to isolate a diastereomer, but rather disclose the use of an acid to form a reducing agent, which is then reacted with an optically active starting compound. In Matsuo et al, there is no isolation of an optically active compound from a mixture of diastereomers. Accordingly, Matsuo et al do not supply the deficiencies of Muller et al.

Further, claims 13 and 14 recite the use of a hydrogen halide as the acid to be used in the isolation. Muller et al and Matsuo et al do not disclose use of such an acid.

In view of the above, applicants submit that Muller et al and Matsuo et al do not disclose or render obvious the subject matter of the above claims and, accordingly, request withdrawal of this rejection.

Claims 47-54 have been rejected under 35 U.S.C. § 103(a) as obvious over Muller et al, optionally in view of Matsuo et al.

Applicants submit that Muller et al and Matsuo et al do not disclose or render obvious the subject matter of the above claims and, accordingly, request withdrawal of this rejection.

Claims 47-54 are directed to an optically active  $\alpha$ -substituted aminoketone of formula (4) or an optically active  $\alpha$ -substituted aminoketone salt represented by formula (5).

The Examiner states that Muller et al disclose, at page 451, lines 11-21, compounds that are structurally similar to those of the present claims. The Examiner states that the difference between Muller et al and the presently claimed compounds is that Muller et al do not disclose optical isomerism of the compounds.

The Examiner argues that it would have been obvious to obtain stereoisomers of the compounds. The Examiner states that Matsuo et al specifically teach a process for obtaining optically active compounds. The Examiner states that Muller et al also use stereoselection, as disclosed at page 451, line 6.

As discussed above, Matsuo et al disclose the use of methanesulfonic acid as a reactive ingredient which reacts with an organoaluminum compound of general formula (4) of Matsuo et al and an alcohol compound of general formula (6) of Matsuo et al to form a reducing agent. This reducing agent is then reacted with an optically active aminoketone starting compound of general formula (1) of Matsuo et al to form an aminoalcohol of general formula (7) of Matsuo et al. Matsuo et al do not disclose or suggest that the method they disclose can be used to form an optically active  $\alpha$ -substituted aminoketone of formula (4) or an optically active  $\alpha$ -substituted aminoketone salt of formula (5).

As set forth in the present specification, an optically active compound represented by formula (4) or (5) with R<sup>1</sup> representing a C<sub>1</sub>-C<sub>4</sub> alkyl group or a C<sub>7</sub>-C<sub>12</sub> aralkyl group is a new molecular entity not disclosed in any literature heretofore.

In view of the above, applicants submit that Muller et al and Matsuo et al do not disclose or render obvious the subject matter of the above claims and, accordingly, request withdrawal of this rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.


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